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EASTMAN

October 3, 2002

Ms. Christine Todd Whitman, Administrator
U.S. EPA
P.O. Box 1473
Merrifield, VA 22116

ORIGINAL

Attn: Chemical Right-to-Know Program

RE: HPV Chemical Challenge Program, AR-201

Dear Ms. Whitman:

This letter is submitted by Eastman Chemical Company ("Eastman") in response to comments received from the Environmental Protection Agency ("EPA") dated September 23, 2002 following EPA's review of the test plan and robust summaries for Ethylene glycol diacetate (EGD; CAS No.: 11-55-7). I would like to thank the EPA for its review and welcome the recognition of its completeness and fulfillment of Eastman's obligation to this chemical in the HPV program.

Below are the EPA's comments to our test plan and various robust summaries, and our responses:

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

1. "Adequate data are available for all endpoints for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

1. "Adequate data are available for photodegradation and stability in water."

2. *"Fugacity.* The submitter used estimated input properties rather than available measured properties. The use of measured input values is strongly recommended. "

The original summary was based on an older version of EPWIN, I have updated the summary's distribution percentages using a newer version of the model. The new results were only slightly different than the previous values and are also based on default values obtained from the EPIWIN program. Fugacity distribution results garnered by performing the above recommendation would not be expected produce significantly different distribution percentages compared to those already presented. Results from this model will vary with future model refinements.

3. *"Biodegradation.* The submitted robust summary is based on a secondary source and has few details. The robust summary needs to incorporate details from the original study so that data adequacy can be determined."

The summary we submitted was actually prepared from the primary reference cited in the HSDB. Even though the information summarized was extracted from the actual publication, the amount of methodology data in the Cain R.B. (1981) article was very minimal. The only methodology detail presented was in a table in which the method utilized was referenced in a footnote. Because of the potential uncertainty in the reliability of the data, it was stated in the robust summary for readers to see the robust summaries that will be submitted for ethylene glycol for more information. It would be readily anticipated that the ester linkages bonding the two acetate units onto the EG molecule would be rapidly degraded in the environment.

Unfortunately, in the context of searching the Cain biodegradation article for more detailed methodology information, a table containing the structure of a chemical they labeled as "ethylene glycol diacetate" was discovered. Interestingly, the structure drawn was not that defined by CAS 111-55-7 as ethylene glycol diacetate, but was a structural isomer with the two acetates connected via an ether linkage rather than through ester bonding. Accordingly, because of the likely mistake in the HSDB, improperly referencing the Cain manuscript as evidence of biodegradability the entire weight of support for this particular endpoint now needs to be derived entirely from ethylene glycol used as a surrogate. It would be readily anticipated that the ester linkage would undergo hydrolysis by microbes in the environment yielding ethylene glycol and two acetates. Environmental fate data will be presented for ethylene glycol in the Ethylene Glycols category of chemicals under the International Council of Chemical Associations (ICCA) High Production Volume (HPV) Initiative.

Ecotoxicity (fish, invertebrates, and algae).

1. "Adequate data are available for these endpoints for the purposes of the HPV Challenge Program."

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

1. "Adequate data are available for the acute and genetic toxicity endpoints. The submitter proposes to use data on ethylene glycol (EG) to support the existing EGD data for the repeated-dose toxicity endpoint and to address the reproductive/developmental toxicity endpoints. The submitter believes that EG is an acceptable surrogate for EGD based on the well-known conversion of alcohol/glycol esters to the parent alcohol/glycol, which is responsible for the systemic toxicity. While EPA agrees that EG is most likely an acceptable surrogate for EGD, the robust summaries for EG are not available (the submitter states that they will be available under the International Council of Chemical Associations (ICCA) High Production Volume Initiative). Consequently, EPA defers judgment on whether the repeated-dose and reproductive/developmental toxicity

endpoints are adequately addressed until the EG robust summaries are available for review."

2. *"Acute Toxicity.* Although the existing study is old and lacks important details, the reported LD50 is supported by the results from the two repeated-dose toxicity studies. No additional testing is necessary."

   " *Acute Toxicity.* Information missing from the robust summary includes the purity of the test material, administered dose in mg/kg, period of post-treatment observation, and method of LD_{50} calculation."

Knowledge regard an absence of purity information was already reflected in the summary. The other requested data were not available in the original reference and accordingly the current summary has not been changed.

3. *Repeated-Dose Toxicity.* Study details missing from the robust summaries are the purity of the test material, method details, numbers of animals per dose level, frequency of data collection, statistical methods, specific hematology and clinical chemistry endpoints, and specific organs that were weighed and examined histopathologically.

Much of the requested data were not available in the original published reports. The main objective of these studies however was to simply demonstrate that EGD induces similar pathological changes as ethylene glycol (EG) in support of our argument that EGD would be metabolized to EG. A more robust assessment of the potential toxicity of EGD should thus be garnered from data that will be presented on EG through the ICCA HPV initiative.

Enclosed with this letter is a computer diskette containing the modified test plan and robust summaries in Adobe Acrobat (.pdf) format. The HPV registration number for Eastman Chemical Company is .

Sincerely,

James A. Deyo, D.V.M., Ph.D., D.A.B.T.
Technical Associate

Enclosure